General

Guideline Title

Evidence-based guideline: treatment of parenchymal neurocysticercosis. Report of the Guideline Development Subcommittee of the American Academy of Neurology.

Bibliographic Source(s)

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

Definitions of the levels of the recommendations (A, B, C, U) and classification of the evidence (Class I-IV) are provided at the end of the "Major Recommendations" field.

In Patients with Symptomatic Intraparenchymal Neurocysticercosis, is Cysticidal Therapy More Effective Than No Therapy, and Does it Affect Long-term Seizure Outcome?

Conclusion

Based on imaging findings in 4 Class I studies (3 concordant, 1 underpowered study failing to show an effect) and a meta-analysis of 2 Class I and 4 Class II studies, albendazole (400 mg twice daily [BID] for adults or weight-based dosing for either adults or children) is probably safe and effective in reducing both the number of cysts and long-term seizure frequency in adults and children with neurocysticercosis. In most studies, corticosteroids were coadministered, in varying dosages, and this combination appears effective. Data are insufficient to indicate whether corticosteroids are necessary in this setting.

Clinical Context

The available studies have used different stratification methods for seizure analysis and different criteria for judging improvement in imaging. On the basis of the 3 Class I studies it appears albendazole plus corticosteroids decreases the number of active brain lesions relative to placebo and, on the basis of a meta-analysis of available data, decreases the number of patients with seizures, at modest cost. These findings appear to be consistent in adults and children.

Recommendation

Albendazole plus either dexamethasone or prednisolone should be considered for adults and children with neurocysticercosis, both to decrease the number of active lesions on brain imaging studies (Level B) and to reduce long-term seizure frequency (Level B).

In Patients with Symptomatic Intraparenchymal Neurocysticercosis, is Treatment with Corticosteroids More Effective Than No Treatment?

Conclusion

On the basis of one Class I study showing no benefit radiologically and ambiguous benefit clinically and one Class II/IV study showing benefit, there is insufficient evidence to recommend steroid treatment alone for patients with solitary intraparenchymal neurocysticercosis granulomata.

Clinical Context

The effect of corticosteroid treatment alone in neurocysticercosis has not been widely studied. Most trials include a combination of cysticidal therapy and steroid treatment.

Recommendation

The evidence is insufficient to support or refute the use of steroid treatment alone in patients with intraparenchymal neurocysticercosis (Level U).

When During the Course of Antiparasitic Treatment Should Steroids be Started?

The Subcommittee found no studies to answer this question.

What is the Efficacy of Antiepileptic Drugs (AEDs) in Treating or Decreasing Occurrence of Subsequent Seizures Secondary to Intraparenchymal Neurocysticercosis, and What is the Optimal Time Course of AED Treatment for Seizures Secondary to Intraparenchymal Neurocysticercosis?

The Subcommittee found no studies to answer this question.

Clinical Context

Given the well-established efficacy and safety of a broad range of AEDs and the frequency with which neurocysticercosis causes seizures, it is reasonable to treat these patients with AEDs at least until the active lesions have subsided.

Definitions:

Classification of Evidence for Therapeutic Intervention

Class I: A randomized, controlled clinical trial of the intervention of interest with masked or objective outcome assessment, in a representative population. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences. The following are also required:

a. Concealed allocation
b. Primary outcome(s) clearly defined
c. Exclusion/inclusion criteria clearly defined
d. Adequate accounting for dropouts (with at least 80% of enrolled subjects completing the study) and crossovers with numbers sufficiently low to have minimal potential for bias.
e. For noninferiority or equivalence trials claiming to prove efficacy for one or both drugs, the following are also required*
    1. The authors explicitly state the clinically meaningful difference to be excluded by defining the threshold for equivalence or noninferiority.
    2. The standard treatment used in the study is substantially similar to that used in previous studies establishing efficacy of the standard treatment (e.g., for a drug, the mode of administration, dose and dosage adjustments are similar to those previously shown to be effective).
    3. The inclusion and exclusion criteria for patient selection and the outcomes of patients on the standard treatment are comparable to those of previous studies establishing efficacy of the standard treatment.
    4. The interpretation of the results of the study is based upon a per protocol analysis that takes into account dropouts or crossovers.

Class II: A randomized controlled clinical trial of the intervention of interest in a representative population with masked or objective outcome assessment that lacks one criteria a–e above or a prospective matched cohort study with masked or objective outcome assessment in a representative population that meets b–e above. Relevant baseline characteristics are presented and substantially equivalent among treatment

groups or there is appropriate statistical adjustment for differences.

Class III: All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome is independently assessed, or independently derived by objective outcome measurement.**

Class IV: Studies not meeting Class I, II, or III criteria including consensus or expert opinion.

*Note that numbers 1-3 in Class Ie are required for Class II in equivalence trials. If any one of the three is missing, the class is automatically downgraded to Class III.

**Objective outcome measurement: an outcome measure that is unlikely to be affected by an observer's (patient, treating physician, investigator) expectation or bias (e.g., blood tests, administrative outcome data).

Classification of Recommendations

Level A = Established as effective, ineffective or harmful (or established as useful/predictive or not useful/predictive) for the given condition in the specified population. (Level A rating requires at least two consistent Class I studies.*)

Level B = Probably effective, ineffective or harmful (or probably useful/predictive or not useful/predictive) for the given condition in the specified population. (Level B rating requires at least one Class I study or two consistent Class II studies.)

Level C = Possibly effective, ineffective or harmful (or possibly useful/predictive or not useful/predictive) for the given condition in the specified population. (Level C rating requires at least one Class II study or two consistent Class III studies.)

Level U = Data inadequate or conflicting; given current knowledge, treatment (test, predictor) is unproven.

* In exceptional cases, one convincing Class I study may suffice for an "A" recommendation if 1) all criteria are met, 2) the magnitude of effect is large (relative rate improved outcome >5 and the lower limit of the confidence interval is >2).

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Intraparenchymal neurocysticercosis

Guideline Category

Assessment of Therapeutic Effectiveness

Management

Treatment

Clinical Specialty

Infectious Diseases

Internal Medicine

Neurology

Pediatrics

Intended Users

Physicians

Guideline Objective(s)

To review the evidence base for different treatment strategies in intraparenchymal neurocysticercosis in adults and children

Target Population

Adults and children with intraparenchymal neurocysticercosis

Interventions and Practices Considered

Albendazole plus either dexamethasone or prednisolone

Note: Steroid treatment alone was considered but not recommended.

Major Outcomes Considered

- Number of remaining active and inactive cysticercal cysts
- Incidence of seizures after treatment
- Side effects of treatment

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Because cysticercosis is quite prevalent in Latin America, a number of relevant studies have been published in the Spanish-language literature. Therefore, a comprehensive search was performed of both English- and Spanish-language articles (with the latter reviewed by 2 panel members who are fluent in Spanish) in Medline, EMBASE, LILACS, and Cochrane Database of Systematic Reviews from 1980 to 2008, using the search terms "neurocysticercosis," "cerebral cysticercosis," "brain cysticercosis," "antiparasitic agents," "antihelmintics," "cysticidal," "clinical trials," "research design," "antiseizure," "anticonvulsant," "antiepileptic," "albendazole," "praziquantel," "steroid," "corticosteroid," "anti-inflammatory agents," "hydrocortisone," "prednisone," "prednisolone," "dexamethasone," and "neurosurgery" (see appendix e-1 for complete search strategy [see the "Availability of Companion Documents" field]). The search identified 590 citations. An updated search of Medline and the Cochrane Database of Systematic Reviews was performed in January 2012 and identified an additional 20 citations.

Number of Source Documents

123

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Classification of Evidence for Therapeutic Intervention

Class I: A randomized, controlled clinical trial of the intervention of interest with masked or objective outcome assessment, in a representative population. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences. The following are also required:

a. Concealed allocation
b. Primary outcome(s) clearly defined
c. Exclusion/inclusion criteria clearly defined
d. Adequate accounting for dropouts (with at least 80% of enrolled subjects completing the study) and crossovers with numbers sufficiently low to have minimal potential for bias.
e. For noninferiority or equivalence trials claiming to prove efficacy for one or both drugs, the following are also required*
    1. The authors explicitly state the clinically meaningful difference to be excluded by defining the threshold for equivalence or noninferiority.
    2. The standard treatment used in the study is substantially similar to that used in previous studies establishing efficacy of the standard treatment (e.g., for a drug, the mode of administration, dose and dosage adjustments are similar to those previously shown to be effective).
    3. The inclusion and exclusion criteria for patient selection and the outcomes of patients on the standard treatment are comparable to those of previous studies establishing efficacy of the standard treatment.
    4. The interpretation of the results of the study is based upon a per protocol analysis that takes into account dropouts or crossovers.

Class II: A randomized controlled clinical trial of the intervention of interest in a representative population with masked or objective outcome assessment that lacks one criteria a–e above or a prospective matched cohort study with masked or objective outcome assessment in a representative population that meets b–e above. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences.

Class III: All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome is independently assessed, or independently derived by objective outcome measurement.**

Class IV: Studies not meeting Class I, II, or III criteria including consensus or expert opinion.

*Note that numbers 1-3 in Class Ie are required for Class II in equivalence trials. If any one of the three is missing, the class is automatically downgraded to Class III.

**Objective outcome measurement: an outcome measure that is unlikely to be affected by an observer's (patient, treating physician, investigator) expectation or bias (e.g., blood tests, administrative outcome data).

Methods Used to Analyze the Evidence

Meta-Analysis

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Each abstract was reviewed by at least 2 reviewers. Review articles without primary data, case reports, and small case series were discarded. The remaining pertinent 123 articles were reviewed in detail, and data regarding cohort size, patient characteristics, inclusion and exclusion criteria, completion rate, treatment and dosage, study design, study length, primary and secondary outcomes, efficacy, and effect size were extracted from each article and tabulated using a data extraction form. Each article was classified according to the American Academy of Neurology (AAN) therapeutic classification of evidence scheme (see the "Rating Scheme for the Strength of the Evidence" field).

Risk differences with 95% confidence intervals (CIs) were used as the preferred measure of effect and statistical precision. When necessary to increase statistical precision, studies with the lowest risk of bias were pooled in a fixed-effects meta-analysis. Class II studies were included in the meta-analysis only when precision was insufficient after Class I studies were pooled.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

For this evidence-based guideline, the Guideline Development Subcommittee (GDS) asked the following question:

- In patients with symptomatic intraparenchymal neurocysticercosis, is cysticidal therapy more effective than no therapy, and does it affect long-term seizure outcome?
- In patients with symptomatic intraparenchymal neurocysticercosis, is treatment with corticosteroids more effective than no treatment?
- When during the course of antiparasitic treatment should steroids be started?
- What is the efficacy of antiepileptic drugs (AEDs) in treating or decreasing occurrence of subsequent seizures secondary to intraparenchymal neurocysticercosis, and what is the optimal time course of AED treatment for seizures secondary to intraparenchymal neurocysticercosis?

Recommendations are based on the strength of the evidence (see the "Rating Scheme for the Strength of the Recommendations" field).

Rating Scheme for the Strength of the Recommendations

Classification of Recommendations

Level A = Established as effective, ineffective or harmful (or established as useful/predictive or not useful/predictive) for the given condition in the specified population. (Level A rating requires at least two consistent Class I studies.*)

Level B = Probably effective, ineffective or harmful (or probably useful/predictive or not useful/predictive) for the given condition in the specified population. (Level B rating requires at least one Class I study or two consistent Class II studies.)

Level C = Possibly effective, ineffective or harmful (or possibly useful/predictive or not useful/predictive) for the given condition in the specified population. (Level C rating requires at least one Class II study or two consistent Class III studies.)

Level U = Data inadequate or conflicting; given current knowledge, treatment (test, predictor) is unproven.

* In exceptional cases, one convincing Class I study may suffice for an "A" recommendation if 1) all criteria are met, 2) the magnitude of effect is large (relative rate improved outcome >5 and the lower limit of the confidence interval is >2).

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Drafts of the guideline have been reviewed by at least 3 American Academy of Neurology (AAN) committees, a network of neurologists, Neurology peer reviewers, and representatives from related fields.

The original guideline document was accepted for publication by the Guideline Development Subcommittee on July 14, 2012; by the Practice Committee on July 24, 2012; and by the AAN Board of Directors on December 26, 2012.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate management of patients with intraparenchymal neurocysticercosis

Potential Harms

Side Effects of Therapy

- Side effects of albendazole plus corticosteroids appear minimal. Of greatest concern has been the potential—emphasized in a single large study—for increased seizures and encephalopathy as a result of treatment-induced parasite death.
- Only 2 studies, detailed other side effects. In the first study headaches occurred in 32 of 60 patients given treatment vs in 31 of 60 controls; dizziness occurred in 9 patients vs in 4, and abdominal complaints occurred in 8 vs in 0.

Qualifying Statements

Qualifying Statements

This statement is provided as an educational service of the American Academy of Neurology (AAN). It is based on an assessment of current scientific and clinical information. It is not intended to include all possible proper methods of care for a particular neurologic problem or all legitimate criteria for choosing to use a specific procedure. Neither is it intended to exclude any reasonable alternative methodologies. The AAN recognizes that specific patient care decisions are the prerogative of the patient and the physician caring for the patient, based on all of the circumstances involved. The clinical context section is made available in order to place the evidence-based guideline(s) into perspective with current practice habits and challenges. Formal practice recommendations are not intended to replace clinical judgment.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Patient Resources

Quick Reference Guides/Physician Guides

Slide Presentation

Staff Training/Competency Material

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Baird RA, Wiebe S, Zunt JR, Halperin JJ, Gronseth G, Roos KL. Evidence-based guideline: treatment of parenchymal neurocysticercosis: Report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology. 2013 Apr 9;80(15):1424-9. [14 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2013 Apr 9

Guideline Developer(s)

American Academy of Neurology - Medical Specialty Society

Source(s) of Funding

This guideline was developed with financial support from the American Academy of Neurology (AAN). None of the authors received reimbursement, honoraria, or stipends for their participation in development of this guideline.

Guideline Committee

Guideline Development Subcommittee of the American Academy of Neurology (AAN)

Composition of Group That Authored the Guideline

Guideline Authors: Ruth Ann Baird, MD; Sam Wiebe, MD; Joseph R. Zunt, MD, MPH; John J. Halperin, MD, FAAN; Gary Gronseth, MD,

FAAN; Karen L. Roos, MD, FAAN

2011–2013 American Academy of Neurology (AAN) Guideline Development Subcommittee (GDS) Members: John D. England, MD, FAAN (*Chair*); Cynthia Harden, MD (*Vice-Chair*); Melissa Armstrong, MD; Eric Ashman, MD; Misha-Miroslav Backonja, MD; Richard L. Barbano, MD, PhD, FAAN; Diane Donley, MD; Terry Fife, MD, FAAN; David Gloss, MD; John J. Halperin, MD, FAAN; Cheryl Jaigobin, MD; Andres M. Kanner, MD; Jason Lazarou, MD; Steven R. Messé, MD, FAAN; David Michelson, MD; Pushpa Narayanaswami, MD, MBBS; Anne Louise Oaklander, MD, PhD, FAAN; Tamara Pringsheim, MD; Alexander Rae-Grant, MD; Michael Shevell, MD, FAAN; Theresa A. Zesiewicz, MD, FAAN; Jonathan P. Hosey, MD, FAAN (*Ex-Officio*); Stephen Ashwal, MD, FAAN (*Ex-Officio*); Deborah Hirtz, MD, FAAN (Ex-Officio)

Financial Disclosures/Conflicts of Interest

Disclosure

R.A. Baird has no disclosures to report. S. Wiebe has received honoraria from UCB Pharma Inc. and has received research funding from Alberta Heritage Medical Research Foundation, Canadian Institute for Health Research, MSI Foundation of Alberta, and the Hotchkiss Brain Institute of the University of Calgary. J.R. Zunt has received honoraria from the American Academy of Neurology (AAN) and has received funding from the National Institutes of Health (NIH) on retroviral infections. J. Halperin has testified in several physician medical malpractice cases and aided the Connecticut Department of Health in proceedings regarding Lyme disease. G. Gronseth has served on a speakers' bureau for Boehringer Ingelheim (resigned December 2011), and receives honoraria from the AAN. K. Roos has received funding for travel from the AAN as a member of its Board of Directors. Go to Neurology.org for full disclosures.

Conflict of Interest

The AAN is committed to producing independent, critical, and truthful clinical practice guidelines (CPGs). Significant efforts are made to minimize the potential for conflicts of interest to influence the recommendations of this CPG. To the extent possible, the AAN keeps separate those who have a financial stake in the success or failure of the products appraised in the CPGs and the developers of the guidelines. Conflict of interest forms were obtained from all authors and reviewed by an oversight committee before project initiation. AAN limits the participation of authors with substantial conflicts of interest. The AAN forbids commercial participation in, or funding of, guideline projects. The AAN Guideline Author Conflict of Interest Policy can be viewed at www.aan.com.

Guideline Endorser(s)

American Epilepsy Society - Disease Specific Society

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: A list of American Academy of Neurology (AAN) guidelines, along with a link to a Portable Document Format (PDF) file for this guideline, is available at the AAN Web site.

Print copies: Available from the AAN Member Services Center, (800) 879-1960, or from AAN, 201 Chicago Avenue South, Minneapolis, MN 55415.

Availability of Companion Documents

The following are available:

- Evidence-based guideline: Treatment of parenchymal neurocysticercosis. Data supplement (e-appendices, e-tables). Available from the American Academy of Neurology (AAN) Web site.

- Evidence-based guideline: Treatment of parenchymal neurocysticercosis. Case presentation. St. Paul (MN): American Academy of Neurology. 2013. 3 p. Available in Portable Document Format (PDF) from the AAN Web site ☐.
- Treatment of parenchymal neurocysticercosis. AAN summary of evidence-based guideline for clinicians. St. Paul (MN): American Academy of Neurology. 2013. 2 p. Available in PDF from the AAN Web site ☐.
- Evidence-based guideline: Treatment of parenchymal neurocysticercosis. Slide presentation. St. Paul (MN): American Academy of Neurology. 2013. Available from the AAN Web site ☐.
- Evidence-based guideline: Treatment of parenchymal neurocysticercosis. CME course. Available online to subscribers of Neurology at the Neurology Web site ☐.
- AAN guideline development process [online]. St. Paul (MN): American Academy of Neurology. Available from the AAN Web site ☐.

Patient Resources

The following is available:

- Neurocysticercosis. Summary of evidence-based guideline for patients and their families. St. Paul (MN): American Academy of Neurology (AAN). 2013. 2 p. Available in Portable Document Format (PDF) from the American Academy of Neurology (AAN) Web site ☐.

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NGC Status

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